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# The Pointer Syndrome: A New Syndrome With Skeletal Abnormalities, Camptodactyly, Facial Anomalies, and Feeding Difficulties

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**We describe a brother and sister with a unique combination of skeletal findings including camptodactyly (phalangeal dislocations), facial anomalies, neonatal respiratory problems, and feeding problems due to poor suck. Metaphyseal splaying, osteopenia, endosteal bone apposition, campomelia, and multiple fractures characterize the other skeletal abnormalities. The parents are first cousins once removed and are unaffected. These cases appear to represent a previously undescribed autosomal recessive disorder. Am. J. Med. Genet. 68:225–230, 1997**


**KEY WORDS: skeletal abnormalities; camptodactyly; neonatal feeding difficulties**

## INTRODUCTION

A large number of syndromes with musculoskeletal changes and camptodactyly have been described and reviewed extensively [Temtamy and McKusick, 1978; Rozin et al., 1984; Emery and Rimoin, 1990]. These disorders include diverse conditions such as Tel Hashomer camptodactyly, Weaver syndrome, the arthrogryposes, and pseudodiastrophic dysplasia. Here we describe sibs from a consanguineous mating with skeletal abnormalities, camptodactyly, facial anomalies, and respiratory and neonatal sucking difficulties. We propose that these patients have a previously undescribed autosomal recessive syndrome.

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## CLINICAL REPORTS

### Patient 1

The propositus is a male born at 38 weeks of gestation to parents who are first cousins once removed. When questioned as to ethnicity, the parents reported having relatives in North and South America and Europe. They speak English and a language that they describe as a mixture of Greek and Italian.

The propositus developed respiratory distress after the first feeding and was transferred to our center with aspiration pneumonia at 2 weeks of age. Birth weight was 2630 g (10th centile). At 2 weeks of age, length was 49.5 cm (25th centile) and head circumference (OFC) was 35 cm (50th centile). He also had moderate micro-retrognathia, high arched palate, relatively small mouth with limitation of opening, "box-shaped" nasal bridge, prominent nasal tip, anteverted nares, hypertelloric appearance, down-slanting palpebral fissures, hypoplastic and low-appearing supraorbital ridge, pectus excavatum, camptodactyly of the second, third, and fourth fingers, and resting extension of the index fingers creating a "pointing" appearance. Neurologic examination was nonfocal but remarkable for irritability and mild hypertonicity. A diagnosis of Weaver syndrome was considered initially, but was excluded because of no significant advancement of bone age and the subsequent clinical course. Chromosomes were normal (46,XY).

Feeding difficulties, apparently present since birth, were due to poor suck. A computed tomography (CT) scan of the brain was normal. Cineradiographic swallowing study showed extremely poor oral phase of swallow but normal pharyngeal and esophageal phases. An upper gastrointestinal series showed moderate gastroesophageal reflux. These findings and recurrent pneumonias necessitated surgical placement of a gastrostomy tube and Nissen fundoplication at age 6 weeks. At 3 months, a tracheostomy was performed for upper airway management. The tracheostomy tube was maintained until 8 months.

At 10 weeks, a fracture of the right humerus was noted. Radiographs of the long bones showed significant

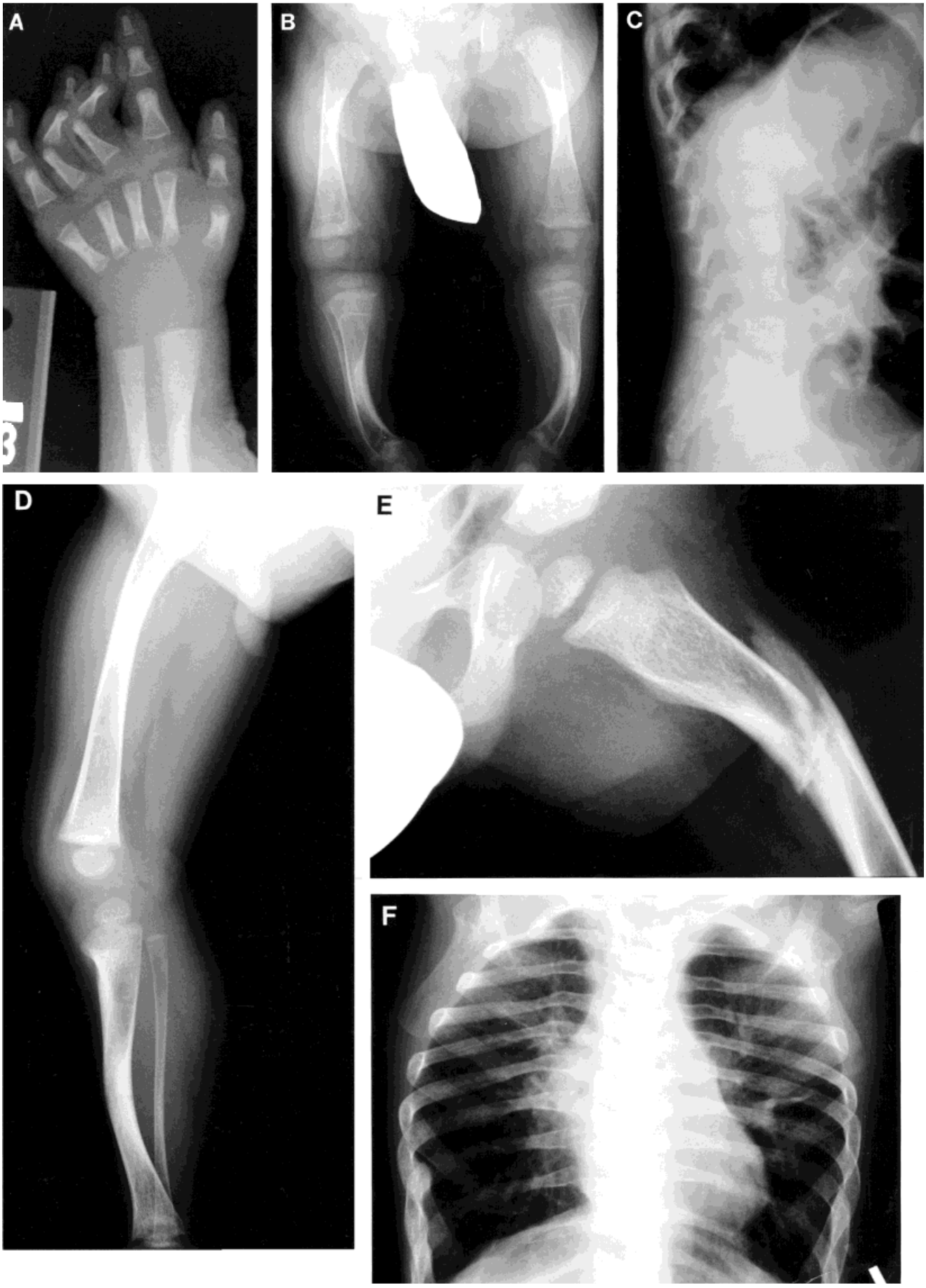


Fig. 1.

osteopenia, mild shortness, metaphyseal splaying, and moderate bowing that had progressed when compared with radiographs obtained at 3 weeks of age. Results of diagnostic evaluation for osteogenesis imperfecta, vitamin D metabolism defect, and Fanconi syndrome were negative. Collagen studies on cultured fibroblasts showed no abnormality in the structure and biosynthesis of type I or type III collagen. Serum calcium, phosphorus, and 25-OH vitamin D levels were normal. Serum amino acids, urine amino acids, and urine organic acids were also normal. At 4 months, he developed a fracture of the left radius. He continued to develop further bowing of the legs and other bony changes (Fig. 1).

After the initial hospitalization, the patient was lost to follow-up for 2 years until the birth of his sister. The propositus at age 30 months is shown in Figure 2. At this time his length was 71 cm (<5th centile), weight was 9.8 kg (<5th centile), and OFC was 47.5 cm (10th centile). The parents reported that the patient started walking at 1 year and began to run at 30 months. At this time he was not climbing stairs. He was able to feed himself with a spoon. He would say more than 10 words that only the family could understand. He was still partially fed by gastrostomy tube and appeared to have delayed speech development. Formal developmental assessment was declined; we suspect that there is mild developmental delay and problems with speech articulation.

He sustained a spontaneous fracture of left femur in the play room during a hospital admission for pneumonia at 2.5 years of age. A few weeks later, he was again admitted to our center with intestinal obstruction and multiple abdominal fistulae requiring surgery. His current hospital course is prolonged with difficulty in wound healing, failure of abdominal fistulae to close, and respiratory failure from infections requiring multiple antibiotic therapies and mechanical ventilation.

### Patient 2

The younger sister of the propositus was born near term following an uneventful pregnancy. Her weight was 2600 g (5th centile), length was at the 10th centile, and OFC at the 25th centile. She had a similar facial appearance as her brother and bilateral camptodactyly of the second, third, and 4th fingers and "pointing" of her index fingers (Fig. 3). At birth her father recognized the "pointing" of her index fingers and her appearance similar to that of her brother. She was transferred to our facility for respiratory distress after being fed; she did not suck throughout her hospitalization. Fundoplication and gastrostomy tube placement were performed at age 1 month. Roentgenographs showed similar skeletal findings as her brother (Fig. 4). A CT scan of the brain, electromyography and nerve conduction studies in upper limbs, and rectus muscle biopsy did not document any abnormalities. Chromosomes were normal (46,XX). Fluorescent in situ hybridization with a probe for the velo-cardio-facial syndrome critical region on chromosome 22 was normal. She died suddenly at home at approximately 6 weeks during an apparent episode of upper respiratory infection. A coroner's autopsy documented pneumonia as the cause of death.

Fig. 1. Radiographs of patient 1. **A**: Left hand. Phalangeal dislocations and camptodactyly at 3 weeks of age. **B**: Lower limbs. Osteopenia, hypoplastic pelvis, rhizomelia-mesomelia, angulated diaphysis, and metaphyseal flaring at age 6 months. **C**: Vertebrae. Abnormal rounded shape at 28 months. **D**: Right lower limb at 28 months. **E**: Left femur. Pathologic fracture at 31 months. **F**: Chest films at 28 months demonstrating mild anterior flare and abnormal angulation (perhaps secondary to rib fractures) of ribs.

TABLE I. Radiographic Findings in Pointer Syndrome

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| Important findings |
| Camptodactyly, phalangeal dislocations |
| Lateral and anterior bowing of tibiae |
| Metaphyseal widening of long bones |
| Round vertebral bodies |
| Generalized osteoporosis |
| Other findings |
| Pathologic fractures |
| Mild shortness of long bones |
| Mild rib flaring |

## DISCUSSION

The sibs reported here have abnormalities of the skeletal, respiratory, and nervous systems (Tables I and II). From the investigation so far, no clue for the pathogenesis of the skeletal changes has been found. They have some signs of pseudodiastrophic dysplasia [Eteson et al., 1986], notably spine and hand changes, but the characteristic proximal femur shape seen in pseudodiastrophic dysplasia was not present in our patients. Some physical and radiographic findings were also similar to those of Weismann-Netter syndrome [Robinow and Johnson, 1988], which is a rare heritable dysplasia with anterior bowing of tibiae and fibulae as well as cortical hyperostosis on the concave side of the curvature but without camptodactyly. Patients with Pyle disease and other craniotubular dysplasias have gross metaphyseal expansion as seen in our patients [Beighton, 1987]; however, unlike our patients, they do not have spine changes or camptodactyly. Our patients' clinical findings also have some similarities to those seen in other camptodactyly syndromes [Temtamy and McKusick, 1978; Rozin et al., 1984]; however, our patients have a novel constellation of findings not seen in these other conditions.

TABLE II. Clinical Findings in Pointer Syndrome

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|---|
| Neonatal respiratory problems |
| Feeding problems due to absent or poor suck |
| Camptodactyly of second, third, and fourth fingers,with pointing appearance of index fingers evident at birth |
| Progressive bowing of limbs, especially legs |
| Facial anomalies |
| Microretrognathia, "box-shaped" nasal bridge, prominent nasal tip, anteverted nares, hyperteloric appearance, down-slanting palpebral fissures, and hypoplastic and low-appearing supraorbital ridge |
| Pathologic fractures |
| ?Developmental delay |
| ?Frequent infections |

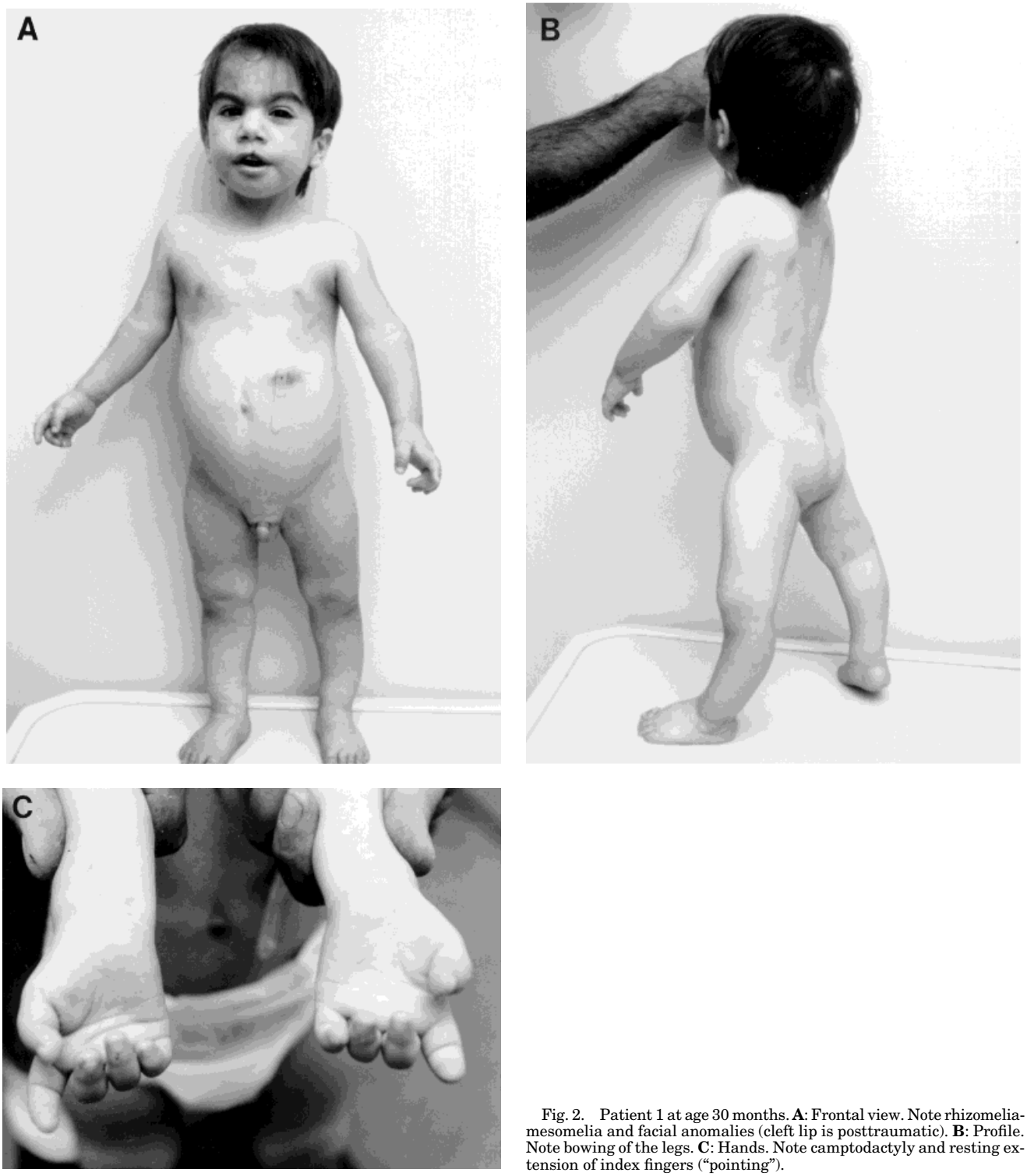


Fig. 2. Patient 1 at age 30 months. **A**: Frontal view. Note rhizomelia-mesomelia and facial anomalies (cleft lip is posttraumatic). **B**: Profile. Note bowing of the legs. **C**: Hands. Note camptodactyly and resting extension of index fingers ("pointing").

The cause of the extremely poor oral phase of swallowing remains unclear. There is no evidence of any structural abnormalities causing difficulty in sucking. Imaging studies did not demonstrate any cerebral or brain stem abnormalities. Normal electromyography (EMG) and nerve conduction studies of the upper limb excluded any generalized muscle or peripheral nerve disorder. However, electrophysiologic studies such as EMG of facial, lingual, and pharyngeal muscles, brain stem evoked potentials, and blink reflexes were not performed in our patients, so we cannot rule out functional abnormalities of the cranial nerve nuclei and brain stem.

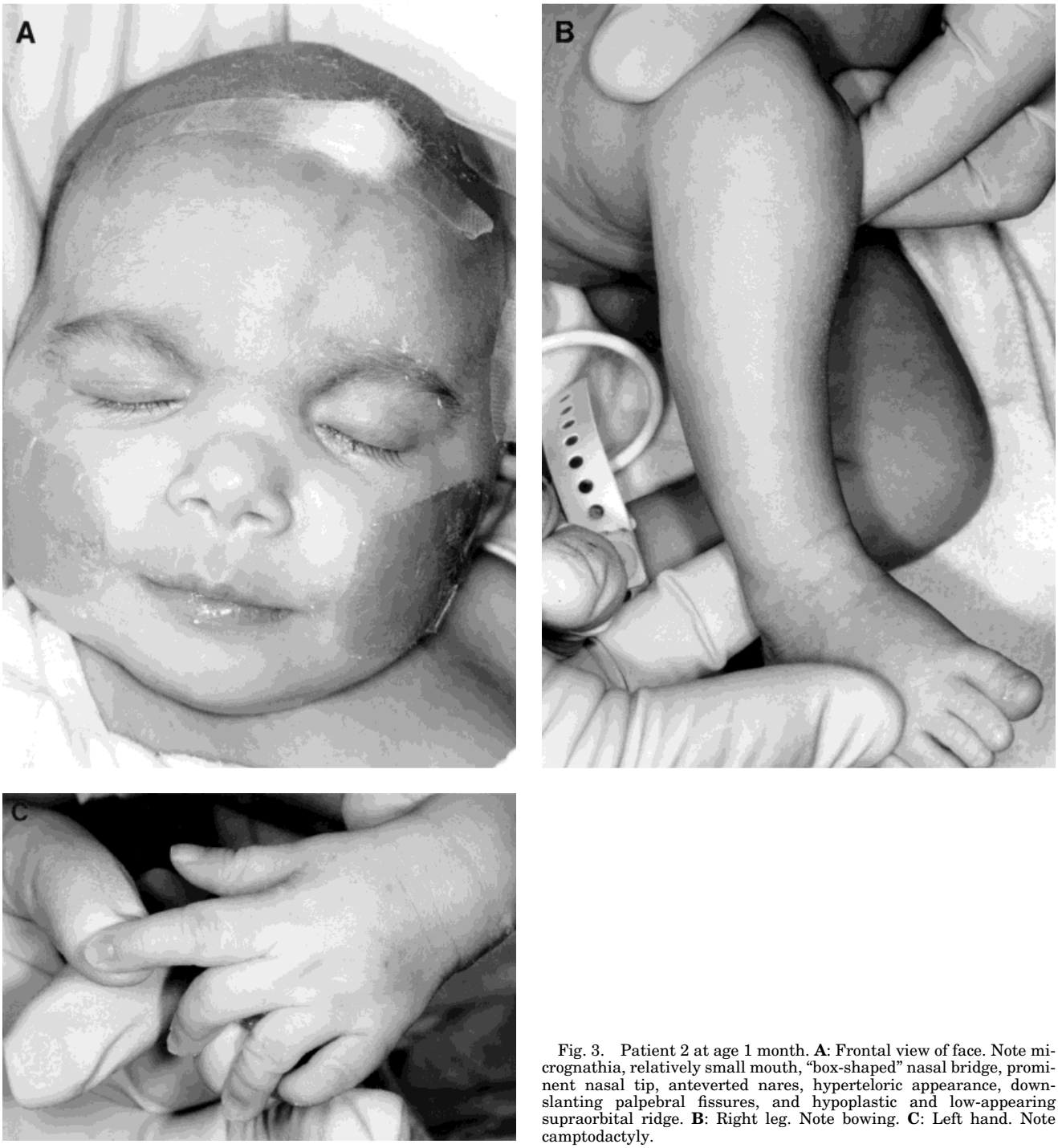


Fig. 3. Patient 2 at age 1 month. **A**: Frontal view of face. Note micrognathia, relatively small mouth, "box-shaped" nasal bridge, prominent nasal tip, anteverted nares, hyperteloric appearance, downslanting palpebral fissures, and hypoplastic and low-appearing supraorbital ridge. **B**: Right leg. Note bowing. **C**: Left hand. Note camptodactyly.

The sudden death of the younger sister of pneumonia and the prolonged hospital course of the propositus with healing problems and frequent pulmonary infections might indicate an immune defect. One recognizable skeletal dysplasia with immune dysfunction is metaphyseal chondrodysplasia, McKusick type, in which there is a prominent T cell defect [Polmar and Pierce, 1986]. A detailed immune work-up was not done in our patients. The surviving sib is chronically and critically ill, and the nature of the immune defect, if any, remains unknown.

To our knowledge, a similar syndrome has not been described. A review of P.O.S.S.U.M., On Line Mendelian Inheritance in Man, and The London Dysmorphology Database did not reveal any similar entity. Despite the large number of syndromes with camptodactyly and the large number of syndromes with skeletal abnormalities, the combination of camptodactyly, progressive skeletal

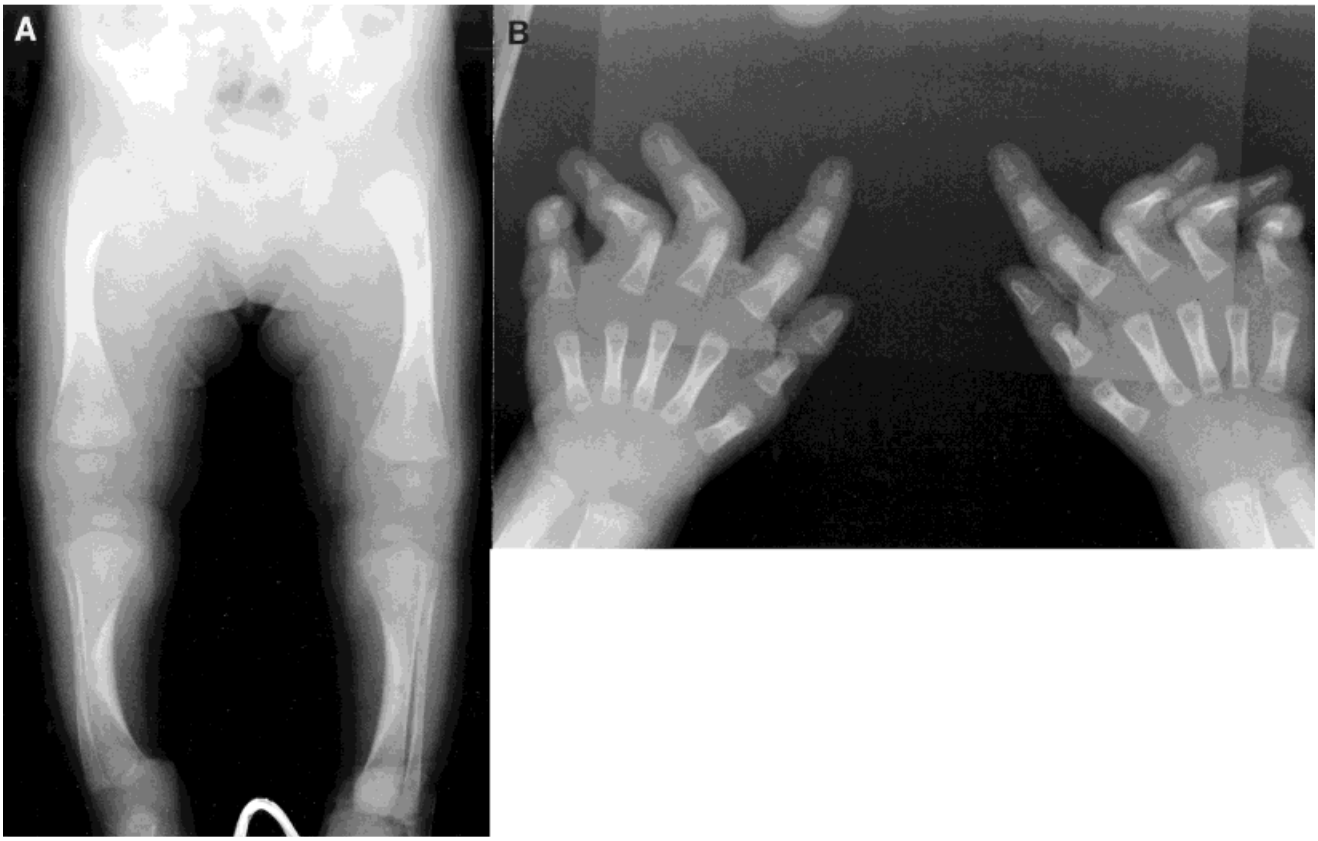


Fig. 4. Roentgenograms of patient 2 at age 4 weeks. **A**: Pelvis and lower limbs. Metaphyseal flare and bowing. **B**: Hands. Camptodactyly, phalangeal dislocations.

changes, particular facial anomalies, and neonatal sucking difficulty appears to be unique. We propose that this syndrome be called "Pointer syndrome" because of the appearance of the hands that was recognizable to both medical personnel and family members.

The ethnic origin of the family was never disclosed directly. The language spoken by the family, the reported geographic distribution of relatives, and our observation of a communal and/or extended family living arrangement leads us to suspect that they are of Gypsy/Roma descent. The occurrence of this disorder in two sibs whose parents are consanguineous suggests autosomal recessive inheritance, although a dominant condition resulting from gonadal mosaicism in one of the parents remains a possibility. Further reports of similarly affected individuals will help to clarify and delineate this condition and its inheritance.

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